

Application No. 10/600,303
 Amendment dated May 17, 2006
 Reply to Office Action of February 17, 2006

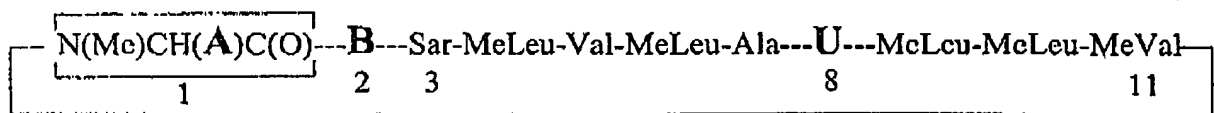
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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application.

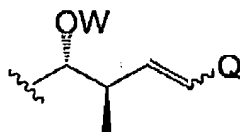
1. (Currently amended) A cyclosporin analog compound of formula I or a pro-drug or a pharmaceutically acceptable salt thereof:



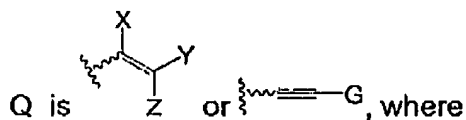
I)

and

A is of the formula:



wherein:



- i) X is selected from hydrogen, halogen, C₁-C₆ alkyl, or aryl;
- ii) one of Y and Z is selected from: hydrogen, deuterium, halogen, or methyl and the other is independently selected from:
 - a) halogen;
 - b) R₁, where R₁ is selected from:
 - 1) hydrogen;
 - 2) deuterium;
 - 3) C₁-C₆ alkyl, optionally substituted with halogen, TMS, aryl, heterocycloalkyl, or heteroaryl;
 - 4) C₂-C₆ alkenyl, optionally substituted with halogen, TMS, aryl, heterocycloalkyl, or heteroaryl;

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- 5) C_2-C_6 alkynyl, optionally substituted with halogen, TMS, aryl, heterocycloalkyl, or heteroaryl;
- 6) C_3-C_{12} cycloalkyl;
- 7) substituted C_3-C_{12} cycloalkyl;
- 8) aryl;
- 9) substituted aryl;
- 10) heterocycloalkyl;
- 11) substituted heterocycloalkyl;
- 12) heteroaryl; or
- 13) substituted heteroaryl;
- c) $-C(O)OR_1$, where R_1 is as previously defined;
- d) $-C(O)OCH_2-V-R_1$, where R_1 is as previously defined and V is $-O-$ or $-S-$;
- e) $-C(O)N(R_3)(R_4)$, where R_3 and R_4 are independently selected from R_1 as previously defined;
- f) $-C(O)SR_1$, where R_1 is as previously defined;
- g) $-C(O)OCH_2OC(O)R_1$, where R_1 is as previously defined;
- h) $-C(S)OR_1$, where R_1 is as previously defined;
- i) $-C(S)SR_1$, where R_1 is as previously defined;
- j) R_2 , where R_2 is selected from:
 - 1) C_1-C_6 alkyl- $M-R_1$, where R_1 is as previously defined and M is absent or selected from:
 - i. $-NH-$;
 - ii. $-N(CH_3)-$;
 - iii. $-S-$;
 - iv. $-S(O)_n-$, where $n = 0, 1, \text{ or } 2$; or
 - v. $-O-$;
 - 2) C_2-C_6 alkenyl- $M-R_1$, where R_1 and M are as previously defined; or
 - 3) C_2-C_6 alkynyl- $M-R_1$, where R_1 and M are as previously defined;

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k) Or in the alternative, Y and Z are taken together with the carbon atom to which they are attached to form a C₃-C₁₂ cycloalkyl moiety; and

ii) G is independently selected from halogen, TMS, R₁ or R₂ as previously defined;

B is selected from:

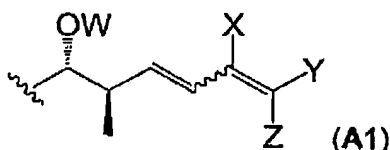
- i) - α Abu-;
- ii) -Val-;
- iii) -Thr-; or
- iv) -Nva-;

U is selected from:

- i) -(D)Ala-;
- ii) -(D)Ser-;
- iii) -[O-(2-hydroxyethyl)(D)Ser]-;
- iv) -[O-(acyl)(D)Ser]-; or
- v) -[O-(2-acyloxyethyl)(D)Ser]-; and

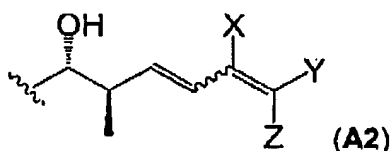
W is selected from hydrogen or a hydroxy protecting group.

2. (Currently amended) A compound of formula I according to claim 1, wherein A is of the formula A1:



where W, X, Y, and Z are as previously defined in claim 1.

3. (Currently amended) A compound of formula I according to claim 1, wherein A is of the formula A2:



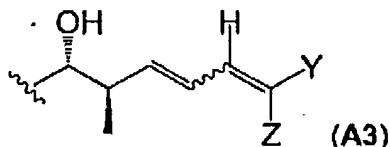
where X, Y, and Z are as previously defined in claim 1.

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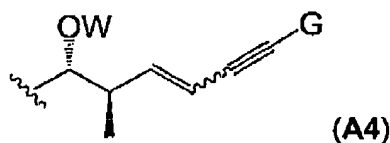
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4. (Currently amended) A compound of formula I according to claim 1, wherein A is of the formula A3:



where Y and Z are as previously defined in claim 1.

5. (Currently amended) A compound of formula I according to claim 1, wherein A is of the formula A4:



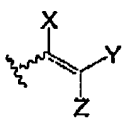
where W and G are as previously defined in claim 1.

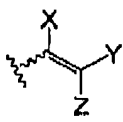
6. (Currently amended) A compound of formula I according to claim 1, wherein A is of the formula A5:



where G is as previously defined in claim 1.

7. (Currently amended) A compound of formula I, according to claim 1, selected from:
 Example 1[.]: A compound of formula I, wherein A is of the formula (1-2) and W is Ac;

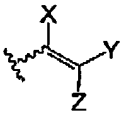
Example 2[.]: A compound of formula I, wherein Q is , W is Ac and X=Y=Z = hydrogen;

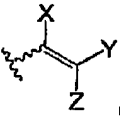
Example 3[.]: A compound of formula I, wherein Q is , W is H and X=Y=Z = hydrogen;

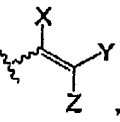
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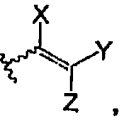
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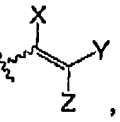
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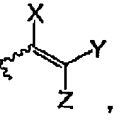
Example 4[.]: A compound of formula I, wherein Q is , Y is CH₃, and W=X=Z = hydrogen;

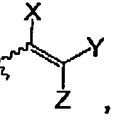
Example 5[.]: A compound of formula I, wherein Q is , Y=Z=CH₃, and W=X=hydrogen;

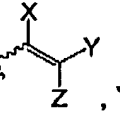
Example 6[.]: A compound of formula I, wherein Q is , Y is -(CH₂)₃CH₃, and W=X=Z = hydrogen;

Example 7[.]: A compound of formula I, wherein Q is , Y is -(CH₂)₂Br, and W=X=Z = hydrogen;

Example 8[.]: A compound of formula I, wherein Q is , Y is *ortho*-Me-phenyl, and W=X=Z = hydrogen;

Example 9[.]: A compound of formula I, wherein Q is , Y is *ortho*-Br-phenyl, and W=X=Z = hydrogen;

Example 10[.]: A compound of formula I, wherein Q is , Y is -CO₂Me, and W=X=Z = hydrogen;

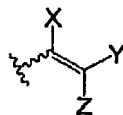
Example 11[.]: A compound of formula I, wherein Q is , Y is *meta*-CHO-phenyl, and W=X=Z = hydrogen;

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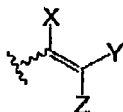
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Example 12[.]: A compound of formula I, wherein Q is



, Y is Et, and
W=X=Z=hydrogen;

Example 13[.]: A compound of formula I, wherein Q is



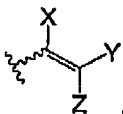
, Y is $-\text{CH}=\text{CHCH}_2\text{TMS}$,
and W=X=Z=hydrogen;

Example 14[.]: A compound of formula I, wherein Q is



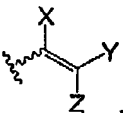
, G is H, and W is H;

Example 15[.]: A compound of formula I, wherein Q is



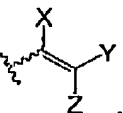
, Y is propyl, and W = X =
Z = hydrogen;

Example 16[.]: A compound of formula I, wherein Q is



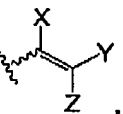
, Y is cyclopropyl, and W
= X = Z = hydrogen;

Example 17[.]: A compound of formula I, wherein Q is



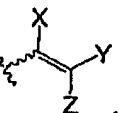
, Y is $-\text{CH}=\text{CHCH}_3$, and
W = X = Z = hydrogen;

Example 18[.]: A compound of formula I, wherein Q is



, X = Y = CH_3 , and W = Z
= hydrogen;

Example 19[.]: A compound of formula I, wherein Q is



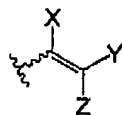
, W = X = Y = hydrogen,
and Z = CH_3 ;

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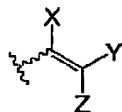
Example 20[.]: A compound of formula I, wherein Q is



, Y is p-bromophenyl, and

W = X = Z = hydrogen;

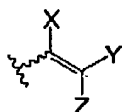
Example 21[.]: A compound of formula I, wherein Q is



, W = X = Y = hydrogen,

and Z = -CH₂CH=CH₂;

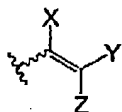
Example 22[.]: A compound of formula I, wherein Q is



, W = X = Y = hydrogen,

and Z is ethyl;

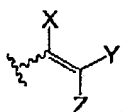
Example 23[.]: A compound of formula I, wherein Q is



, W = X = Y = hydrogen,


and Z = -CH=CHCH₃;

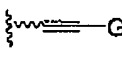
Example 24[.]: A compound of formula I, wherein Q is




, W = X = Y = hydrogen,

and Z = -CH₂OCH₃;

Example 25[.]: A compound of formula I, wherein Q is , G = -CH=CHCH₃ and W = hydrogen;

Example 26[.]: A compound of formula I, wherein Q is , G = propyl and W = hydrogen; or

Example 27[.]: A compound of formula I, wherein Q is , G = -CH₃ and W = hydrogen.

8. (Currently amended) A pharmaceutical composition comprising a therapeutically effective against immune disorders amount of at least one compound of Formula (I) in

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claim 1, or a pharmaceutically acceptable salt, ester or prodrug thereof, in combination with a pharmaceutically acceptable carrier or excipient.

9. (Previously presented) A method of treating organ transplantation rejection in a subject, which comprises administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 8.
10. (Previously presented) A method of treating an immune disorder in a subject, which comprises administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 1.
11. (Previously presented) The method of claim 10, wherein said immune disorder is selected from the group consisting of: rheumatoid arthritis, inflammatory bowel disease, psoriasis, asthma, atopic dermatitis, allergic rhinitis, and chronic obstructive pulmonary disease.
12. (Previously presented) A method of treating an immune disorder in a subject, which comprises topically administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 1.
13. (Previously presented) The method of claim 12, wherein said inflammatory or immune disorder is selected from the group consisting of psoriasis and eczema.
14. (Previously presented) The method of claim 12, wherein said topically administering is achieved via inhalation.
15. (Previously presented) The method of claim 14, wherein said inflammatory or immune disorder is an obstructive airways disease.

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16. (Previously presented) The method of claim 15, wherein said airways disease is selected from the group consisting of asthma, allergic rhinitis, bronchitis, cystic fibrosis, and chronic obstructive pulmonary disease.
17. (Previously presented) The method of claim 16, wherein said chronic obstructive pulmonary disease is emphysema or chronic bronchitis.
18. (Cancelled)
19. (Cancelled)
20. (New) A pharmaceutical composition comprising at least one compound of Formula (I) in claim 1, or a pharmaceutically acceptable salt, ester or prodrug thereof, in combination with a pharmaceutically acceptable carrier or excipient.